Notice of Allowability	Application No.	Applicant(s)	
	09/780,438	QI, XIAOYANG	
	Examiner	Art Unit	
	Sheridan K Snedden	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *11/19/2003*.
2. ☒ The allowed claim(s) is/are *1-44*.
3. ☒ The drawings filed on *09 February 2001* are accepted by the Examiner.
4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.
5. ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
   (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

8. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No. ____.
   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
   (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the margin according to 37 CFR 1.121(d).

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1☐ Notice of References Cited (PTO-892)
2☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No. _____
4☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5☐ Notice of Informal Patent Application (PTO-152)
6☐ Interview Summary (PTO-413), Paper No._____ .
7☒ Examiner's Amendment/Comment
8☒ Examiner's Statement of Reasons for Allowance
9☐ Other .

EXAMINER'S AMENDMENT

Response to Amendment

1. This Office Action is in response to paper filed 19 November 2003. Applicant's amendment of claims 16-31, 33-34, 37, 39-42 is acknowledged.

2. Applicant's amendment to the specification appearing as a duplicate in paper filed 19 November 2003 is acknowledged.

3. Groups I-III, claims 1-44, directed to an allowable product composition and related methods are rejoined and considered. Claims 1-44 are under examination.

Withdrawal of Objections and Rejections

4. The objections and/or rejections not explicitly restated or stated below are withdrawn.

Claim Amendments

5. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Karlyn A. Schnapp on January 28, 2004.

The application has been amended as follows:

1. (currently amended) A method for delivering a pharmaceutical agent through a membrane, wherein the method comprises applying to said membrane a composition comprising:

a. anionic phospholipid;

b. a safe and effective amount of the pharmaceutical agent contained within the aqueous interior of the phospholipids; and

c. a fusogenic protein or polypeptide derived from prosaposin

in a pharmaceutically acceptable carrier, wherein the concentration of the fusogenic protein or polypeptide is of a sufficient amount to deliver the pharmaceutical agent through the membrane.

2. (original) The method of claim 2 wherein the concentration of phospholipids are in at least a 10-fold excess, by weight, to that of the fusogenic protein or polypeptide.

3. (original) The method of claim 2 wherein the pH of the composition is between about 5.5 and 2.

4. (original) The method of claim 3 wherein the anionic phospholipid is an anionic liposome.

5. (original) The method of claim 4 wherein the fusogenic protein or polypeptide is associated with the liposome through an electrostatic and hydrophobic interaction.

6. (original) The method of claim 5 wherein the membrane is selected from the group consisting of dermal and mucosal membranes.

7. (currently amended) The method of claim 6 wherein the fusogenic protein or polypeptide is selected from the group consisting of saposin A, saposin C, ~~polypeptide analogs, derivatives, homologues, fragments of saposin A and saposin C,~~ and mixtures thereof.

8. (currently amended) The method of claim 6 wherein the fusogenic protein or polypeptide is saposin C.

9. (currently amended) The method of claim 6 wherein the fusogenic protein or polypeptide is ~~SEQ. ID. NO. 1~~ SEQ ID NO: 1.

10. (original) The method of claim 6 wherein the fusogenic protein or polypeptide is ~~SEQ. ID. NO. 2~~ SEQ ID NO: 2.

11. (currently amended) The method of claim 6 wherein the fusogenic protein or polypeptide is selected from the group consisting of those proteins or polypeptides ~~of the formula~~ given by ~~SEQ ID Nos. 3-6~~ SEQ ID NO: 3-6.

12. (original) The method of claim 7 wherein administration of the composition is via a transdermal patch.

13. (original) The method of claim 7 wherein the composition is administered either enterally or topically.

14. (currently amended) A method for delivering a pharmaceutical agent through either a dermal or mucosal membrane, wherein the method comprises the administration to said membrane of a composition comprising:

a. anionic liposomes;

b. a safe and effective amount of the pharmaceutical agent contained within the aqueous interior of the liposomes; and

c. saposin C;

in a pharmaceutically acceptable carrier, wherein the concentration of the liposomes are of a sufficient amount to deliver a safe and effective amount of the pharmaceutical agent through the membrane, the pH of the composition is between about 5.5 and 2, and the saposin C is associated with the surface of the liposome through an electrostatic and hydrophobic interaction.

15. (original) The method of claim 14 wherein the concentration of the liposomes is in at least a 10-fold excess, by weight, to that of saposin C.

16. 16) (currently amended) A therapeutic phospholipid composition comprising:

a. an anionic phospholipid;

b. a safe and effective amount of the pharmaceutical agent contained within the aqueous interior of the phospholipids; and

c. a fusogenic protein or polypeptide derived from prosaposin;

in a pharmaceutically acceptable carrier, wherein the ~~concentration of the~~ fusogenic protein or polypeptide is present in a sufficient concentration to deliver the pharmaceutical agent through a biological membrane and the fusogenic protein or polypeptide is associated with the phospholipid through an electrostatic and hydrophobic interaction.

17. (currently amended) The therapeutic phospholipid composition of claim 16 wherein the concentration of ~~anioinic~~ anionic phospholipid is in at least a 10-fold excess, by weight, to that of the fusogenic protein or polypeptide.

18. (previously presented) The therapeutic phospholipid composition of claim 17 wherein the pH of the composition is between about 5.5 and 2.

19. (previously presented) The therapeutic phospholipid composition of claim 18 wherein the anionic phospholipid is an anionic liposome.

20. (previously presented) The therapeutic phospholipid composition of claim 19 wherein the biological membrane is selected from the group consisting of dermal and mucosal membranes.

21. (previously presented) The therapeutic phospholipid composition of claim 20 wherein the fusogenic protein or polypeptide is selected from the group consisting of saposin A, and saposin C, and mixtures thereof.

22. (previously presented) The therapeutic phospholipid composition of claim 20 wherein the fusogenic protein or polypeptide is saposin C.

23. (currently amended) The therapeutic phospholipid composition of claim 20 wherein the fusogenic protein or polypeptide is ~~SEQ. ID. NO. 1~~SEQ ID NO: 1.

24. (currently amended) The therapeutic phospholipid composition of claim 20 wherein the fusogenic protein or polypeptide is ~~SEQ. ID. NO. 2~~ SEQ ID NO: 2.

25. (currently amended) The therapeutic phospholipid composition of claim 20 wherein the fusogenic protein or polypeptide is selected from the group consisting of those proteins or polypeptides given by ~~SEQ ID Nos. 3-6~~ SEQ ID NO: 3-6.

26. (previously presented) The therapeutic phospholipid composition of claim 21 wherein the composition is formulated as part of a transdermal patch.

27. (previously presented) The therapeutic phospholipid composition of claim 21 wherein the composition is formulated for enteral or topical administration.

28. (currently amended) An anionic liposomal composition used to deliver a pharmaceutical agent through either a dermal or mucosal membrane, wherein the composition comprises:

a. anionic liposomes;

b. a safe and effective amount of the pharmaceutical agent contained within the aqueous interior of the liposomes; and

c. saposin C;

in a pharmaceutically acceptable carrier where the pH of the composition is between about 5.5 and 2, wherein the concentration of the saposin C is of a sufficient amount to deliver the pharmaceutical agent through a biological membrane and the saposin C is associated with the surface of the liposomes through an electrostatic and hydrophobic interaction.

29. (previously presented) The anionic liposomal composition of claim 28 wherein the concentration of the anionic liposomes is in at least a 10-fold excess, by weight, to that of saposin C.

30. (currently amended) A composition comprising a safe and effective amount of a pharmaceutical agent contained within the aqueous interior of ~~in an~~ anionic liposomes, which are associated with a prosaposin-derived fusogenic protein or polypeptide via an electrostatic and hydrophobic interaction, wherein the concentration of the fusogenic protein or polypeptide is of a sufficient amount to deliver the pharmaceutical agent through a biological membrane, the

composition contained in a pharmaceutically acceptable carrier, wherein the pH of the composition is between about 5.5 and 2.

31. (previously presented) The composition of claim 30 wherein the concentration of anionic liposomes is in at least a 10-fold excess, by weight, to that of the fusogenic protein or polypeptide.

32. (Original) The composition of claim 31 wherein the biological membrane is selected from the group consisting of dermal and mucosal membranes.

33. (previously presented) The composition of claim 32 wherein the fusogenic protein or polypeptide is selected from the group consisting of saposin A, saposin C, and mixtures thereof.

34. (previously presented) The composition of claim 31 wherein the fusogenic protein or polypeptide is saposin C.

35. (currently amended) The composition of claim 31 wherein the fusogenic protein or polypeptide is ~~SEQ. ID. NO. 1~~ SEQ ID NO: 1.

36. (currently amended) The composition of claim 31 wherein the fusogenic protein or polypeptide is ~~SEQ. ID. NO. 2~~ SEQ ID NO: 2.

37. 37. (currently amended) The composition of claim 31 wherein the fusogenic protein or polypeptide is selected from the group consisting of those proteins or polypeptides given by ~~SEQ ID Nos. 3-6~~ SEQ ID NO: 3-6.

38. (currently amended) A phospholipid composition used to deliver a pharmaceutical agent through either a dermal or mucosal membrane, wherein the composition comprises:

a. anionic liposomes;

b. a safe and effective amount of the pharmaceutical agent contained within the aqueous interior of the liposomes; and

c. saposin C;

in a pharmaceutically acceptable carrier, wherein the pH of the composition is between about 5.5 and 2, the concentration of the saposin C is of a sufficient amount to deliver the pharmaceutical agent through the membrane and the saposin C is associated with the surface of the liposome through an electrostatic and hydrophobic interaction.

39. (previously presented) The phospholipid composition of claim 38 wherein the concentration of the anionic liposomes is in at least a 10-fold excess, by weight, to that of saposin C.

40. (currently amended) The polypeptide consisting of ~~SEQ. ID. NO. 1~~ SEQ ID NO: 1.

41. (currently amended) The polypeptide consisting of ~~SEQ. ID. NO. 2~~ SEQ ID NO: 2.

42. (currently amended) A compound of the formula consisting of ~~SEQ ID Nos. 3-6~~ SEQ ID NO: 3-6.

43. (currently amended) A method for treating Gauchers Disease wherein the method comprises the administration of a composition comprising:

a. anionic liposomes;

b. a safe and effective amount of acid beta-glucosidase contained within the aqueous interior of the liposomes; and

c. saposin C;

in a pharmaceutically acceptable carrier, wherein the pH of the composition between about 5.5 and 2, the concentration of the saposin C is of a sufficient amount to deliver the pharmaceutical agent through the membrane and the saposin C is associated with the surface of the liposome through an electrostatic and hydrophobic interaction.

44. (original) The method of claim 43 wherein the concentration of the liposome is in at least a 10-fold excess, by weight, to that of saposin C.

Reasons for Allowance

6. The following is an examiner's statement of reasons for allowance: Vaccaro *et al.* at page 184 teach that glucosylceramidase is incorporated into the bilayer of the liposome and not contained within the aqueous interior of the liposome. In addition, a search of the prior art was

absent of any teachings that placed a therapeutic within the aqueous interior of a prosapsoin derived fusogenic liposome for use as a delivery vehicle.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

7. Claims 1-44 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (571) 272-0959. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for regular communications to the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
February 9, 2004
SKS

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER